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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,905	02/23/2006	Colin Watts	FBR0002-100	3003

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COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
HALVORSON, MARK	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,905	WATTS ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,12,19,55 and 75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 12, 19, 55 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/12/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 12, 19, 55 and 75 are pending.

Applicant's election of Group 2 in the reply filed on May 6, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-3, 12, 19, 55 and 75 are under examination.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on pages 11, 93 and 109 of the Specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Figures 19A and 23A of the drawings are written as Figure 19 and Figure 23 in the Brief Description of the Drawings. Appropriate corrections are required.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

Figure 5B lists sequences without SEQ ID NOs..

In response to this office action, Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. The nature of the non-compliance did not preclude an

examination of the elected invention on the merits, the results of which are presented below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 12, 19 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the diagnosis of breast and ovarian cancer and a method for predicting recurrence of ovarian cancer comprising determining the level of EDD protein and the art indicated below, does not reasonably provide enablement for a method of diagnosis of all cancers, a method for predicting recurrence of all cancers or a method for determining predisposition for disease comprising determining the level of protein encoded by nucleic acid linked to map position 8q22.3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a method for diagnosing a cancer or predicting recurrence of a cancer in a subject comprising determining the level of protein encoded by nucleic acid linked to a map position 8q22.3.

The Specification discloses that EDD protein was highly expressed in 63% of breast cancer patients. (page 103). In addition, the Specification discloses that EDD expression ovarian cancer was predictive of relapse (Id).

The art indicates that there are several genes located at map position 8q22.3 including BAALC, CTHRC1, FBX043, RIMS2, and YWHAZ. (chromosome 8, on-line Atlas of Genetics and Cytogenetics in Oncology and Haematology, Auguest 2, 2008). In addition, there are several other genes that are mapped to a region that includes map position 8q22.3 such as eIF4E. The Specification does not disclose whether the

expression of any of these genes are upregulated in cancer. The prior art discloses that BAALC is upregulated in leukemia and prostate cancer (Tanner et al. (US Patent Application Publication 2003/ 0119043, published June 26, 2003, priority filing date November 9, 2001) and that eIF4E was upregulated in breast cancer. (Sorrells et al, Annals Surgical Oncol, 1997, 5:232-237).

One cannot extrapolate the teaching of the specification to the enablement of the claims because the specification does not provide examples or guidance for a method for predicting recurrence of all cancers or a method for determining predisposition for disease comprising determining the level of protein encoded by nucleic acid linked to map position 8q22.3. The specification only demonstrates that EDD protein is overexpressed in breast and ovarian cancer and predicted the recurrence of ovarian cancer. The specification does not provide a nexus between the method for diagnosing all cancers, comprising determining the level of proteins encoded by nucleic acid linked to a map position 8q22.3 of the human geneome and the overexpression of EDD protein in ovarian and breast cancer. The specification does not provide a nexus between the method for determining the recurrence of all cancers, comprising determining the level of proteins encoded by nucleic acid linked to a map position 8q22.3 of the human geneome and the finding that EDD expression was predictive of relapse of ovarian cancer. The specification does not provide a nexus between the method for determining the predisposition to all cancers comprising determining the level of proteins encoded by nucleic acid linked to a map position 8q22.3 of the human geneome and the overexpression of EDD protein in ovarian and breast cancer.

Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders and associated markers such as CIN and HLA alleles and HPV type. Tockman et al teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials

(see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). In addition, Slamon et al. (Science Vol. 235, January 1987, pages 177-182) teach other essential factors that are known to be important in the prognosis of breast cancer in individual patients such as size of the primary tumor, stage of the disease at diagnosis, hormonal receptor status, and number of axillary lymph nodes involved with disease (page 178, 1st column, 2nd paragraph). Such data are critical to assessing actuarial curves for relapse (Figure 3), and for comparing disease-free survival and overall survival to prognostic factors (Table 4). It is clear that the art teaches the necessary experimentation and data required to allow one of skill in the art to predict the method of therapeutic follow up, prognosis and the diagnosis of relapse. In the present case, Applicants have only demonstrated that the overexpression of EDD protein case is indicative of breast and ovarian cancer and that that EDD expression was only predictive of relapse in ovarian cancer.

The present claims are drawn to a method for detecting any cancer by determining the expression product of a nucleic acid that is linked to map position 8q22.3of the human genome, which is the map position for several genes expressing proteins other than EDD. Cancers comprise a broad group of malignant neoplasms divided into two categories, carcinoma and sarcoma. The carcinomas originate in

epithelial tissues while sarcomas develop from connective tissues, see Taber's Cyclopedic Medical Dictionary (1985, F.A. Davis Company, Philadelphia, p. 274). Given that not all cancers originate from the same tissue types, it is expected and known that cancers originate from different tissue types have different structures as well as etiologies and would present differently. Thus, it would not be predictably expected that a nexus, for example drawn to a connection between EDD protein expression and cancer would be established between cancer types that arose from different tissue types. Further, it is well known that even two carcinomas that present on the same organ have significant differences in etiology and genetic constitution. For example, Busken, C et al, (Digestive Disease Week Abstracts and Itinerary Planner, 2003, abstract No: 850), teach that there is a difference in COX-2 expression with respect to intensity, homogeneity, localization and prognostic significance between adenocarcinoma of the cardia and distal esophagus, suggesting that these two cancers have different etiology and genetic constitution (last five lines of the abstract). Additionally, Kaiser (Science, 2006, 313, 1370) teaches that in a genomic analysis of mutations in breast and colon cancers, it was found that the cancer genes differ between each colon and breast cancers and each tumor had a different pattern of mutations. Kaiser teaches that the steps to cancer may be more complex than had been anticipated, see 3rd col.

Given the disclosure of the specification and the teaching in the art that indicates the unpredictability of detecting a cancer biomarker between different types of cancer and the disclosure that there are many genes linked to map position 8q22.3, one skilled in the art could not predictably diagnose any cancer by determining the level of an expression product of a nucleic acid that is linked to map position 8q22.3 of the human genome or even more specifically, EDD.

Therefore, in view of the breadth of the claims, lack of guidance in the specification, the absence of working examples, and the state of the art, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Tanner et al. (cited previously).

Claim 1 is drawn to a method for detecting a cancer in a subject comprising determining the level of protein encoded by nucleic acid linked to a map position 8q22.3 of the human genome, wherein the cancer cell is epithelial in origin.

Tanner et al disclose that Brain and Acute Leukemia, Cytoplasmic (BAALC) (located at 8q22.3 of the human genome – Atlas of Genetics and Cytogenetics in Oncology and Haematology) is overexpressed in leukemia and prostate cancer. (paragraphs 112 to 126).

Claim 75 is rejected under 35 U.S.C. 102(e) as being anticipated by Callaghan et al. (US 7,105,652, issued Sept 12, 2006, filed April 20, 1998).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim 75 is drawn to a method for determining the ability of a cell to phosphorylate CHK2 in response to a DNA damaging agent comprising determining the level of expression of EDD in the cell. The active step is determining the expression of EDD in a cell.

Callaghan et al disclose determining the expression of EDD protein in transfected HEK cell sand in normal breast and breast cancer epithelial cells. (column 13, lines 25-32).

Claims 1-3, 12 and 19 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sorrells et al, (cited previously).

The claims are drawn to a method for detecting a cancer in a subject comprising determining the level of protein encoded by nucleic acid linked to a map position 8q22.3. of the human genome, wherein the cancer cell is from a cancer selected from the group consisting of ovarian cancer, melanoma, metastatic melanoma, squamous cell carcinoma of the head and neck, squamous cell carcinoma of the tongue, hepatocellular carcinoma, breast cancer, a metastases of ovarian cancer, a metastases of melanoma, a metastases of metastatic melanoma, a metastases of squamous cell carcinoma of the head and neck, a metastases of squamous cell carcinoma of the tongue, a metastases of hepatocellular carcinoma and a metastases of breast cancer.

Sorrells et al disclose that eIF4E (linked to a map position 8q22 -q23 of the human genome – Atlas of Genetics and Cytogenetics in Oncology and Haematology) was overexpressed in breast cancer samples. (page 234, 2nd paragraph to page 235, 1st paragraph). The gene eIF43 has not been precisely mapped but eIF43 has been mapped to a region in chromosome 8 that includes 8q22.3.

Summary

No claims allowed.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson
Patent Examiner
571-272-6539

/MISOOK YU/
Primary Examiner, Art Unit 1642